MI vs controls. For *HindIII*, the homozygote (−/−) frequency also was not increased in MI (8.7%, OR = 1.1) or CAD pt (8.3%, OR = 0.88).

Conclusion: Common LPL polymorphisms are not associated with large increases in risk (OR > 1.5) for CAD or MI. However, smaller overall risk, or subgroup specific risks (ie, in women), are not excluded, and should be further evaluated.

1065-13 Isomorphic Species of Atherogenic Lipoprotein (a) and its Relationship With Coronary Artery Disease Clinical Severity

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The relationship between atherogenesis and thrombogenesis is well established and widely recognized. The plasma level of lipoprotein (a) - Lp(a) - has a direct involvement on the pathophysiology of coronary artery disease (CAD), through its dual role as a transport and interaction particle on the endothelial wall. We assume that the higher the plasma level of Lp(a) and smaller the molecular structure of apoprotein (a) - Apo (a), more easily Lp(a) can express its pathogenic effect. Iso Lp(a) was evaluated in a population of 43 pts with clinical diagnosis of CAD, mean age 72 ± 8 yrs (55–81 yrs), 40% male gender, divided according to increasing degrees of CCS classification and the presence of acute myocardial infarction (AMI). Atherogenic Lp(a) was identified, genetically determined with several isomorphic forms - Iso Lp(a) - which were defined in terms of the number of kringles. IsoLp(a) can be divided in two groups, depending on its dimensions and penetrating capacity of the endothelial wall. IsoLp(a) with small dimensions (Group I; n = 20 pts) - IsoLp(a) F, B, S1 and S2- represent the particles with higher penetrating capacity in the arterial wall, while the IsoLp(a) with greater dimensions and lower penetrating capacity - IsoLp(a) S3, S4 and S < 4 - were included in the second group (Group II; n = 23 pts). IsoLp(a) are detected by specific and highly selective biochemical technique followed by immunoblotting and enzymatic detection. Total Cholesterol (Chol), LP rich in Chol (LDL, HDL, HDL2), Lp(a) and anti-phospholipid anti-bodies (APA) were determined.

	CCS < 2	CCS > 3	AMI	Lp(a)	Col/HDL	HDL	HDL2	APA
Group I	0%	55%	45%	49 ± 25	5.2 ± 1.4	46 ± 12	15 ± 8	11 ± 8
Group II	21%	58%	31%	13 ± 16	5.4 ± 1.8	48 ± 11	16 ± 6	6 ± 8
p Value	0.01	ns	0.01	< 0.001	ns	ns	ns	0.001

The isomorphic species in circulating Lp(a) with small dimensions have a higher atherogenic potential that is directly related with its penetrating capacity and accumulation within the arterial wall. Patients with more severe clinical expression of CAD have more frequent small isomorphic Apo (a) and this could have patho-physiologic implications in the progression and growing of intra-coronary atheromatous lesions.

1065-14 Human Paraoxonase (PONA) Genotype Determines the Susceptibility to Oxidation of High-Density Lipoprotein (HDL) Particle

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Background: PONA is a HDL associated enzyme that hydrolyze organphosphates, carboxylic acids ester, and carbamate. Recently the association of coronary artery disease (CAD) and PONA activity were reported, and PONA genotype is considered as a new coronary risk factor. In this study we investigated the PONA genotype and susceptibility to oxidation of lipoproteins to elucidate the contribution of PONA to atherosclerosis.

Methods: We analyzed 134 patients who underwent coronary angiography in our hospital. DNA were obtained from patients blood and PCR-RFLP methods were used to determine the Gln/Arg polymorphism of PONA. Genotype frequency of A/A, A/B, B/B were 26.9%, 35.1%, 38.1%, respectively. Lipoproteins were obtained from patients at least 12 hours fasting and were separated with sequential ultracentifugation. We analyzed TBARS and the continuous monitoring of copper induced oxidation using 5 μM CuSO4 and 100 μg protein of each lipoproteins at 37C among the groups of three genotype.

Results: TBARS levels of plasma, VLDL, and LDL did not differ among the groups, but HDL TBARS were significantly higher in A/A than A/B or B/B (1.013, 0.616, 0.582 nM MDA/mg protein, p = 0.014). In A/A, LDL lag-time was slightly shorter than A/B or B/B (43.2, 48.6, 48.0 min., p = 0.051), also HDL lag-time was significantly shorter than A/B or B/B (18.4, 21.9, 20.1 min., p = 0.005). There was no difference of CAD prevalence among the groups (A/A = 75%, A/B = 74%, B/B = 65%).

Conclusion: PONA genotype clearly determined the oxidative modification of HDL particle. Although we failed to confirm the association of PONA genotype and CAD in the present study, PONA may play a role in pathogenesis of atherosclerosis via HDL oxidation.

1065-15 Lipoprotein Lipase Gene Polymorphisms: Associations With Coronary Artery Disease and Lipoprotein Levels in Japanese Population

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Background: In some previous studies, several restriction fragment length polymorphisms (RFLPs) in the lipoprotein lipase (LPL) gene were associated with coronary artery disease (CAD) and plasma lipid levels, but it is less clearly established in Japanese population. In this study, we examined the distribution of the LPL polymorphisms in a Japanese population and the associations between LPL polymorphisms (Hind III, Pvu II) and CAD, plasma lipid levels.

Methods: All patients (n = 209, 168 males) were underwent coronary angiography. CAD+ was defined as ≥50% setnosis in at least one of major branch of coronary artery (CAD+ = 148). The Hind III/Pvu II genotypes were analyzed by PCR RFLPs.

Results: The frequencies of the H2 and P2 alleles ("2" denotes presence of cutting site) were 0.80 and 0.76, respectively. The H2H2 genotype was significantly more frequent in CAD+ than CAD− ($P < 0.01$). The Pvu II polymorphism showed no significant associations with CAD. H2H2 genotype associated with significantly lower levels of HDL ($P < 0.05$) and Apo AI ($P < 0.05$) than H1H2 + H1H1 genotype. (43 ± 16 versus 50 ± 21 mg/dl [mean ± SD] and 112 ± 23 versus 122 ± 26 mg/dl, respectively). P2P2 genotype had also significantly lower levels of HDL ($P < 0.05$) and Apo AI ($P < 0.01$) than P1P2+P2P2 genotype (43 ± 16 versus 50 ± 20 mg/dl and 112 ± 22 versus 123 ± 26 mg/dl, respectively). There were no other associations between LPL RFLPs and other lipoprotein components.

Conclusions: The results suggest that Hind III polymorphism in the LPL gene contributes to HDL cholesterol levels and development of CAD.

1065-16 Recombinant Apolipoprotein A-I$_{Milano}$ Protects Against Lysophosphatidylcholine-induced Endothelial Dysfunction

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We previously demonstrated antiatherogenic effects of reconstituted high density lipoprotein (HDL) using the recombinant apolipoprotein (apo) A-I mutant, apoA-I$_{Milano}$ (ApoM), complexed with the phospholipid carrier DMPC. In this study, we examined whether ApoM has any effects on lysophosphatidylcholine (LPC)-induced impairment of endothelium-dependent vasodilatation. Responses to acetylcholine (1 μM) were examined in carotid arteries from 15 normal rabbits perfused in vitro before and after incubation with LPC (50 μM) in absence and presence of apoM and wild-type apo A-I (ApoWT) complexed with DMPC, plasma-derived HDL, free apoM (F-ApoM) (all 1 mg/ml) and the carrier DMPC (30 μg/ml). Changes in diameter were measured, and responses were expressed as % change in diameter (mean ± SD) of preconstricted arteries. Baseline diameter of carotid arteries was 2.9 ± 0.1 mm. *p < 0.05 versus-LPC control.

	Control	ApoM	ApoWT	HDL	F-ApoM	DMPC
LPC	83 ± 7	80 ± 14	76 ± 16	75 ± 11	77 ± 22	81 ± 22
+LPC	29 ± 21*	58 ± 22	46 ± 26	38 ± 35	22 ± 2*	24 ± 25*
N	9	9	8	5	5	5

LPC had no effects on sodium nitroprusside-mediated vasodilatation.

Conclusion: Apo A-I$_{Milano}$ and apo A-I wild-type-reconstituted HDL as well as plasma-derived HDL, but not free apoM or the carrier DMPC, significantly attenuated LPC-induced impairment of endothelium-dependent vasodilatation. The protective effects of apoM and apoWT were more pronounced than plasma HDL. Thus, reversal of endothelial dysfunction by HDL may, in part, explain the inverse relationship between HDL cholesterol and coronary heart disease.

1065-17 Familial Hypercholesterolemia: The Limited Predictive Value of Plasma LDL-Cholesterol

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Background: Demonstration of a mutation in the LDL-receptor gene confirms

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the diagnosis Familial Hypercholesterolemia (FH). To assess the predictive value of the serum LDL-cholesterol only, the following study was conducted.

Methods: Blood samples were prospectively collected on 990 consecutive participants in the Dutch National Screening program for FH. Persons receiving treatment for hypercholesterolemia were not included. Both plasma LDL-cholesterol measurement and DNA analysis were executed in all blood samples.

Results: 325 (33%) carried a mutation in LDL receptor gene while 21% of these had a LDL-cholesterol *below* the 95th percentile for sex and age. In the non-carriers, 14% had a LDL-cholesterol *above* the 95th percentile.

	< 95th percentile	> 95th percentile
All carriers (n = 325)	256 (78.8%)	69 (21.2%)
All non-carriers (n = 665)	96 (14.4%)	569 (85.4%)
Carriers < 18 years	70 (92.1%)	6 (7.9%)
Non-carriers < 18 years	10 (13.0%)	67 (87.0%)

sensitivity 0.79 (95% CI: 0.73–0.83), specificity 0.86 (95% CI: 0.83–0.89)

Conclusion: The diagnosis of FH by determination of plasma LDL-cholesterol only is inaccurate and leads to unnecessary misdiagnosis (14% false-positive) while at the same time a substantial number of FH patients is not detected (21% false-negative) and possibly denied the appropriate therapy.

1066 Dilated and Right Ventricular Cardiomyopathy

Monday, March 30, 1998, 3:00 p.m.–5:00 p.m.
Georgia World Congress Center, West Exhibit Hall Level
Presentation Hour: 3:00 p.m.–4:00 p.m.

1066-23 Tacrolimus-induced Cardiomyopathy: A Systematic Review of Over 3600 Adult Patients

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Background: Tacrolimus is an immunosuppressant used to prevent graft rejection. Recently, several cases of hypertrophic cardiomyopathy (HCM) have been reported in pediatric transplant patients receiving tacrolimus. The purpose of this study was to determine the prevalence and etiology of HCM in non-cardiac adult transplant patients receiving tacrolimus.

Methods: We retrospectively reviewed our transplant database for non-cardiac transplant patients receiving tacrolimus from 1/82 to 4/96. Records of 3609 transplant recipients (liver = 2257; kidney = 1333; other = 19) were reviewed. Patients with left ventricular hypertrophy (LVH) defined as a posterior or septal wall thickness ≥ 1.3 cm. by echocardiography (ECHO) were independently evaluated.

Results: Of 846 patients with ECHOs, 171 had LVH. Patients were categorized on the basis of etiology as valvular disease (37%), hypertensive disease (30%), ischemic heart disease (18%), or multifactorial (15%). Only six patients were identified in whom no underlying cause of HCM was evident.

Conclusion: The prevalence of HCM in our tacrolimus-treated adult transplant population is similar to that reported in general population studies. This data suggests that treatment with tacrolimus is not a risk factor for HCM.

1066-24 Left Atrial Systolic Function Is Depressed in Idiopathic and Preserved in Ischemic Dilated Cardiomyopathy

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Background: Left atrial (LA) myopathy has been suggested in idiopathic (ID) dilated cardiomyopathy (DC). We hypothesized that LA systolic function would be depressed in IDDC compared to ischemic DC (ISDC).

Methods: Seventeen patients with IDDC, 16 with ISDC and 18 age and sex matched controls were studied. LA volumes were echocardiographically determined at mitral valve (MV) opening (maximal, LAmax), electrocardiographic P wave (onset of atrial systole, LAp) and MV closure (LAmin) from the apical 4-and 2-chamber views (biplane area-length method). LA systolic function was assessed with the LA active emptying fraction (ACTEF) = (LAp-LAmin)/LAp. Cardiac catheterization was performed within 24 hours after echocardiography.

Results: see table.

	IDDC	ISDC	Control
LAmax (cm^3/m^2)[a]	44.6 ± 13.6	48.2 ± 18.3	26.9 ± 6.2
LAp (cm^3/m^2)[a]	34.6 ± 13.4	30.8 ± 10.9	16.7 ± 3.7
LAmin (cm^3/m^2)[b]	28.5 ± 11.8	21 ± 9.1	10.7 ± 2.5
ACTEF[c]	0.18 ± 0.1	0.32 ± 0.1	0.36 ± 0.1
LVEDP (mmHg)[a]	16.8 ± 4.5	17.2 ± 6	10 ± 4

a: IDDC = ISDC < Control, p < 0.05; b: IDDC < ISDC < Control, p < 0.05; c: IDDC < ISDC = Control, p < 0.05; LVEDP: Left ventricular end-diastolic pressure

Conclusions: At similar LA loading conditions, LA systolic function is depressed in IDDC and preserved in ISDC suggesting LA myopathy.

1066-25 Influence of Cardiac-Cycle Length on Left Ventricular Ejection Fraction and Filling in Idiopathic Dilated Cardiomyopathy

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Rapid heart rate can affect adversely left ventricular (LV) ejection fraction (EF). In order to determine if resting cardiac-cycle length (CCL, msec) influenced LVEF and filling, resting LVEF, peak filling rate (PFR, stroke volumes/sec) and time to peak filling rate (TPFR, msec) were measured with gated blood-pool radionuclide ventriculography and correlated (Table) with CCL in 60 patients with no cardiac pathology (NORMAL), 38 with idiopathic dilated cardiomyopathy (IDM) confirmed by cardiac catheterization and 23 with reduced LVEF and coronary artery disease (CAD); mean LVEF in these three groups were 0.63 ± 0.06, 0.25 ± 0.11 and 0.24 ± 0.09 respectively and mean CCL was 890 ± 172, 752 ± 161 amd 778 ± 194 respectively.

	NORMAL	IDM	CAD
LVEF	0.26*	0.58	0.38
	0.04	0.0003	0.09
PFR	0.36	0.76	0.51
	0.0006	0.0001	0.03
TPFR	0.23	0.55	0.47
	0.08	0.0008	0.03

* = r value with p value below

It was concluded that in IDM the correlations between CCL, resting VLEF, PFR and TPFR were moderately strong in IDM compared to NORMAL and CAD, despite the similar LVEF in CAD. Thus, a short resting CCL in IDM was associated with reduced LVEF and restrictive filling, whereas a long CCL was associated with preserved LVEF and more normal LV filling. Resting CCL and thus heart rate may be a more critical determinant of resting LV function in IDM than in NORMAL and CAD.

1066-26 Congestive Heart Failure in the Natural History of Arrhythmogenic Right Ventricular Cardiomyopathy

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Arrhythmogenic right ventricular cardiomyopathy (ARVC) is characterized by ominous ventricular arrhythmias due to fibro-fatty replacement of the atrophic myocardium. Pathologic changes can be so widespread to affect the whole RV, with or without left ventricular (LV) involvement, as to determine congestive heart failure (CHF). We reviewed our collection of ARVC hearts to establish clinicopathological features of patients (pts) with CHF. Among 40 cases, 10 (25%) had CHF (5 F, 5 M, age range 28–65, mean 42.3 yrs vs 24.6 of the remaining pts, p < 0.001). Four died because of cardiac arrest (2), cerebral (1) and pulmonary embolism (1); 6 underwent to cardiac transplantation due to refractory CHF. An in vivo ARVC diagnosis was achieved in 6, the remaining 4 were misdiagnosed as dilated cardiomyopathy. Four had previous episodes of systemic embolism. Basal ECG showed atrial fibrillation or flutter in 4, ventricular arrhythmias of left bundle branch block type in 3 and polymorphic in 7, T wave inversion in V1 up to V5 in 5. Mean heart weight was 430 g (range 350–600); RV enlargement was huge in 5 and moderate in 5; RV aneurysms in 8 (80%); mural thrombosis of the RV in 2 and of left atrial appendage in 1. At histology all cases showed transmural fibro-fatty replacement with patchy inflammatory infiltrates. In conclusion, CHF may be the end-point in the natural history of ARVC. Age-dependancy of this clinical outcome supports the theory of an acquired progressive disease. In the setting of biventricular depressed contractility, ARVC may mimic dilated cardiomyopathy and heart transplantation constitutes the only therapeutic option.

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